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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/497,957	02/04/2000	Winston J. Thomas	8907-087-999	8113

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JONES DAY
222 EAST 41ST ST
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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary

Application No.

09/497,957

Applicant(s)

THOMAS ET AL.

Examiner

Jeanine A Goldberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 92-137 is/are pending in the application.
- 4a) Of the above claim(s) 113-123 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 92-112 and 124-137 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 23, 2003. Currently, claims 92-137 are pending. Claims 113-123 have been withdrawn as drawn to non-elected subject matter.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is FINAL.
3. Any objections and rejections not reiterated below are hereby withdrawn.
4. This action contains new grounds of rejection necessitated by amendment.

Election/Restrictions

5. Applicant's election of SEQ ID NO: 1 has been received. Upon review of the instant application and prosecution history, it was unclear why a subsequent restriction was required following the non-final office action mailed on July 16, 2001 which examined SEQ ID NO: 3. As discussed with Roger Rich on March 24, 2004, the previous restriction requirements are withdrawn and prosecution will continue with the instant claims as they correspond to the originally elected SEQ ID NO: 3.
6. Therefore, Claims 92-112, 124-137, as applied to SEQ ID NO: 3 are under examination.

Priority

7. This application claims priority to several applications. The application 08/632,673, filed April 15, 1996 fails to disclose plasmids or SEQ ID NO: 3. Therefore, the instant application appears to receive the benefit of 08/6552,265, filing date May 23, 1996.

Drawings

8. The drawings are acceptable.

New Matter

9. Claims 136 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "a monkey cell" are included. The specification does not describe or discuss "a monkey cell". Instead the specification describes pig, sheep, goat, ape, orangutan, primate. This description does not support monkey. The concept of "pig, sheep, goat, ape, orangutan, primate" does not appear to be part of the originally filed invention. Therefore, "pig, sheep, goat, ape, orangutan, primate" constitutes new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 102-112 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a plasmid comprising an oligonucleotide of at least 8-18 consecutive nucleotides from SEQ ID NO: 3.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’ required a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”. In analyzing whether

the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, Applicant has defined only a fragment from a nucleic acid sequence embedded within a larger sequence. The claims broadly encompass SNPs, variants, splice variants, mutations, translocations etc. of the nucleic acid of SEQ ID NO: 3 in addition to homologues of the sequences from different species of animals which have not been described in the instant specification. Further, an 18-mer embedded within a larger sequence also encompasses post-filing date mouse, rat and pig sequences. The post-filing date art also teaches sequences from humans which were not contemplated at the time the invention was made. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 95, 100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasmids and viral vectors comprising SEQ ID NO: 3, does not reasonably provide enablement for gene therapy vectors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention and breadth of claims

Claims 95, 100 are drawn to viral vectors wherein the viral vector is a gene therapy vector. The invention is an class of invention which the CAFC has characterized as “the unpredictable arts such as chemistry and biology.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The art teaches that in 12 years of gene therapy trials, no gene therapy has been improved. The main problem of gene therapy is the lack of efficient, specific, and safe DNA delivery systems.

Guidance in the Specification.

The specification fails to teach how to use the gene therapy vector for its intended use. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Working Examples

The specification has no working examples of gene therapy.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied. The post filing date art supports that in 2004 gene therapy remains unpredictable and unworkable. Thus, in 1996, at the time the invention was made, it is clear that gene therapy was not predictable. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the use of gene therapy has not been successful in 12 years, a gene therapy vector is not enabled. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner

that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Interpretation

12. It is noted that Claims 124-137 are drawn to a cell comprising the expression plasmid which is an expression vector. The claims are directed to mammalian cells including primate, monkey and human cells. Upon review of the instant specification, it has been determined that the claims do not read on an intact organism and therefore does not read on a human being.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 102-112 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 102-112 are drawn to a plasmid comprising an oligonucleotide of at least 8-18 consecutive nucleotides selected from a sequence "unique" to SEQ ID NO: 3. The use of the word unique in the claims is indefinite. Upon review of the specification, the specification does not teach what a unique sequence encompasses. Based upon the 102 rejection below, it is clear that 8-18 mers are not unique to SEQ ID NO: 3, as

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they appear in additional sequences. Therefore, the metes and bounds of "unique" is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 102-112 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (Genbank Accession Number R47761, May 18, 1995).

As noted above, the word "unique" in the claim does not limit the claim, as it is unclear what a sequence unique to SEQ ID NO: 3 encompasses.

Hillier et al. (herein referred to as Hillier) teaches a nucleic acid in plasmid pT3T3d (Pharmacia). The nucleic acid plasmid comprises approximately 130 consecutive nucleotides of SEQ ID NO: 3 (limitations of Claim 102-112). As seen in the alignment, positions 55-199 of Hillier are 100% identical to SEQ ID NO: 3.

15. Claims 102-112 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier-2 et al. (Genbank Accession Number R07696, April 1995).

As noted above, the word "unique" in the claim does not limit the claim, as it is unclear what a sequence unique to SEQ ID NO: 3 encompasses.

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Hillier-2 teaches a nucleic acid in plasmid pT3T3d (Pharmacia). The nucleic acid plasmid comprises 235 consecutive nucleotides of SEQ ID NO: 3 (limitations of Claim 102-112). As seen in the alignment, positions 1-235 of Hillier are 100% identical to SEQ ID NO: 3.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 92-112, 124-135, 137 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent No. 5,872,237 in view of the specification of 5,872,237.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d

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1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claim 1 of U.S. Patent No. 5,872,237 recites an isolated nucleic acid comprising SEQ ID NO: 20. The instant claim 1(b) recites an isolated nucleic acid comprising SEQ ID NO: 3, which is encompassed by claim 1 of the '237 patent which recites a nucleic acid sequence which comprises SEQ ID NO: 20. SEQ ID NO: 20 has 100% identity over the entire length of SEQ ID NO: 3 of the instant application.

Claim 92-112 differs from Claim 1 herein in that it fails to disclose the nucleic acid within a plasmid. However, the portion of U.S. Patent No. 5,872,237 that supports a plasmid is Column 4. The term "nucleic acids", as used herein, refers to either DNA or RNA. "Nucleic acid sequence" or "polynucleotide sequence" refers to a single- or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases read from the 5' to the 3' end. It includes both self-replicating plasmids, infectious polymers of DNA or RNA and nonfunctional DNA or RNA. Col. 26-28 provide cells including prokaryotic, yeast, insect, mammalian, bacteria etc. Therefore, it would have been obvious to modify the nucleic acid of Claim 1 of U.S. Patent No. 5,872,237 such that the nucleic acid is within a plasmid, vector or host cell.

17. Claims 92-112, 124-135, 137 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1, 2, 4, 24-45 of U.S. Patent No. 6,025,130 in view of the specification of 6,025,130.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claims 1, 2, 4, 24-45 of U.S. Patent No 6,025,130 recites an isolated nucleic acid comprising SE QID NO: 3. The instant claim 1(b) recites an isolated nucleic acid comprising SEQ ID NO: 3, which is encompassed by claim 1 of the '130 patent which recites a nucleic acid sequence which comprises SEQ ID NO: 3. SEQ ID NO: 3 has 100% identity over the entire length of SEQ ID NO: 3 of the instant application.

Claim 92-112 differs from Claim 1 herein in that it fails to disclose the nucleic acid within a plasmid. However, the portion of U.S. Patent No. 6,025,130 that supports a plasmid is Column 4. In accordance with a fourth aspect of the present invention, there is provided an expression vector comprising a coding sequence of a nucleic acid set forth above operably linked with a promoter sequence capable of directing expression of the coding sequence in host cells for the vector. Col. 10-15 teaches that expression systems may include yeast, insect, bird, fish, mammalian, etc. Therefore, it would have been obvious to modify the nucleic acid of Claim 1 of U.S. Patent No 6,025,130 such that the nucleic acid is within a plasmid, vector or host cell.

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Conclusion

18. No claims allowable over the art.

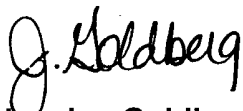
19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jeanine Goldberg

Patent Examiner

March 31, 2004



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